REMARKS

The Official Action dated July 24, 2002 has been carefully considered. Accordingly, the changes presented herewith together with the following remarks, are believed sufficient to place the present application in condition for allowance. Reconsideration is respectfully requested.

In the Official Action, the Examiner further restricted the claims to Group I comprising claims 21-27 and Group II comprising claim 79. During a telephone conversation with Examiner John Sipos, the undersigned elected Group I with traverse. The election is made with traverse on the basis that it would not be unduly burdensome for the Examiner to examine all of the claims in this application as filed. However, the traversal is rendered moot as Applicant has cancelled claims 1-20, 28, 79 and 97-102 without prejudice in order to expedite prosecution of the case. Applicant reserves the right to further pursue the cancelled claims in a divisional application.

Regarding claim 21, Applicant has further added the phrase --by passing the material through the front end opening-- to the step of "filling material into the chamber". Support for this addition can be found, for example, on page 3, lines 27-31. The dependency of claim 27 has been corrected and additional changes to the claims were made to correct minor informalities. The changes to the claims are not believed to introduce new matter to the disclosure.

In the Official Action of July 24, 2002, the Examiner objects to the specification as failing to provide antecedent basis for the claimed subject matter. The paragraph on page 24, beginning on line 21 has been amended to contain language found in original claim 21. No new matter is believed to be involved as the paragraph has been amended to include a description of the originally claimed subject matter. [See MPEP § 608.01(l)]. The paragraph beginning on page 3,

line 24 and the paragraph beginning on page 25, line 5 have also been amended to correct minor informalities and are not believed to involve the introduction of new matter.

Claims 21-27 were rejected by the Examiner as being unpatentable over U.S. Patent No. 5,435,076 to Hjertman. This rejection is traversed and reconsideration is respectfully requested.

Hjertman discloses a process of manufacturing injection cartridges of the dual-chamber type (see column 6, starting at line 48). The Hjertman process includes the step of inserting a movable wall 3 to a predetermined position in relation to a bypass arrangement 4. The front chamber 5 of the cartridge is then filled with a predetermined amount of a solution. The filled cartridge is then placed with the front opening upwards in a suitable tray for freeze-drying. As described in column 7 of Hjertman, an arrangement of cartridges and sleeves with stoppers are introduced into a freeze-drying apparatus and the freeze-drying procedure is carried out. After freeze drying, the front chambers of the cartridges are sealed by inserting the stoppers 11 in the necks 2 of the cartridges. Once the front chambers of the cartridges have been sealed, the cartridges are taken out from the freeze-drying apparatus, and the liquid component is filled into the cartridges through their rear ends, which are subsequently closed by means of the pistons 25.

Hjertman, however, does not appear to teach or suggest the step of inserting the piston through the front end opening as recited in claim 21. In the Official Action dated July 24, 2002, the Examiner apparently argues that insertion of the piston through the front end opening would be obvious since the Examiner states that the Applicant has not disclosed that the use of either opening provides an advantage, is used for a particular purpose, or solves a stated problem. Applicant respectfully traverses this assertion. The description portion of the specification specifically points out the claimed manufacturing process of the present application provides improvements over the cited Hjertman reference, for example, with respect to the manufacture of

ampoules in highly automated processes (see page 2, line 26 through page 3, line 7; in particular page 3, lines 6-7). In addition, the specification also states that the design further facilitates filling operations through the front opening and allows a piston to be inserted through the front opening and not only through the rear opening, which may be used to reduce necessary manufacturing steps and facilitate equipment design by allowing more steps to be conducted from the same side (see page 3, lines 27-31). Indeed, page 25, lines 12-14 describes the process, with reference to FIG. 4, wherein all of the steps up to step 46 inclusive can be conducted from the upper side of the carrier. Therefore, clear advantages are achieved with a process for the manufacture of prefilled syringe type ampoule including the steps of inserting a piston through the front end opening of a barrel, filling material into the chamber by passing the material through the front end opening and sealing the front end opening with a sealer as set forth in claim 21.

Moreover, as illustrated in FIGS. 1, 2 and 4-6 of Hjertman, the outer diameter of the movable wall 3 appears to be significantly greater than the interior diameter of the relatively narrow opening adjacent the neck 2. Thus, Hjertman appears to teach away from inserting the movable wall 3 through that opening due to the inevitable interference between the outer dimension of the movable wall and the inner dimension of the relatively narrow opening. In fact, it appears that the Hjertman barrel profile would necessarily require insertion of the movable wall 3 from the opposite end of the barrel.

It is also noted that FIG. 3 of Hjertman does not appear to depict the actual profile of the barrel 1 since the actual barrel profile would necessarily include the bypass arrangement in order to form a functioning dual chamber cartridge. With respect to FIG. 3, it is also not necessary to illustrate the actual barrel profile since the description of this figure does not even mention the movable wall 3 or its placement but focuses on the modified interior surface of the neck 2 (see

generally at 21 in FIG. 3) and the shape of the stopper 11. Accordingly, it is believed that the actual barrel profile of the embodiment of FIG. 3 corresponds to the barrel profile of FIGS. 1, 2 and 4-6 including a relatively narrow neck opening that would teach away from a process as recited in claim 21 and including the steps of inserting a piston through the front end opening, filling material through the front end opening and sealing the front end opening.

For the reasons stated above, Applicant respectfully requests allowance of claim 21. Applicant further requests allowance of claims 22-27 since these claims depend directly or indirectly from allowable independent claim 21.

It is believed that the above represents a complete response to the outstanding Office action. Reconsideration and early allowance are respectfully requested.

Respectfully submitted,

By Stephen S. Wentsler

Stephen S. Wentsler
Attorney for Applicants
Registration No. 46,403
DINSMORE & SHOHL LLP
1900 Chemed Center
255 East Fifth Street
Cincinnati, Ohio 45202
(513) 977-8683

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VERSION WITH MARKINGS SHOWING CHANGES MADE

In the specification:

Please replace the paragraph from page 3, line 24 through page 5, line 14 with the following paragraph:

--The invention may be used with the already improved syringe type device described, having a sleeve around a central barrel. According to the invention such a device can be still more simplified by using a barrel of substantially the same diameter at its front opening as its overall diameter, allowing use of e.g. a plain cylinder. This design further facilitates filling operations through the front opening but above all allows a piston to be inserted through the front opening and not only through the rear opening, which may be used to reduce necessary manufacturing steps and facilitate equipment design by allowing more steps to be conducted [form] from the same side. The design also makes it easier to use a sealer or stopper for the front opening extending out to and beyond the barrel diameter. In the product this property allows the sealer to better center and buffer the external sleeve and in manufacture the same property makes it possible to grip and hold the sealer in an equipment cavity adapted to the barrel diameter, which in turn may be used to eliminate use of the sleeve for sealer manipulation, making sleeve design more free, e.g. in respect of barrel to sleeve distance, and enabling removal of the sleeve from at least the sterile manufacturing zone and enabling independent inspection of the barrel ampoule semi-manufacture. Use of a barrel with a front opening edge being rounded with the edge material kept within the nominal barrel inner and outer diameters further amplifies these advantages. The property also gives general advantages in bulk or individual handling of the barrels as such, e.g. higher precision and strongly reduced risk for damage and particle release. Sealers and stoppers can more easily and without tumbling risks be attached to the opening with mechanized means, also in the absence

of the sleeve as sealer manipulator, and the stoppers as such can be made less elaborate and with less cavity forming parts within the barrel. The invention also provides an ampoule carrier giving substantial general advantages in manufacture of prefilled ampoules. The carrier can be used in most manufacturing steps, reducing bulk treatment and corresponding damage risks for the ampoules. The carrier provides one or more channels for individual ampoules. Channels formed as a cavities in a carrier body and essentially surrounding the ampoule give a protection and contamination confinement similar to the known sleeve. The cavity has been found to assist in a uniform heat conduction and radiation shielding of special importance in lyophilizing processes. If desired the cavity can be made to radially support an ampoule over substantial length and the structure can be made, e.g. by spacers or otherwise, to accommodate ampoules of different lengths or widths, thereby providing a valuable versatility. Although not restricted to any particular ampoule form the structure cooperates beneficially with ampoules of the general cylindrical form described. A channel made longer than the ampoule can be used to hold a sealer in a floating, and yet protected, position above but concentric with the ampoule opening for later individually centered and guided axial movement into a closed position, an option of particular value in lyophilization, for allowing first vapor passage past the sealer and later in-situ closure of the powder chamber. When used with a cylindrical barrel type ampoule and slightly oversized sealer as described, these advantages can be obtained with maintained possibilities for ampoule introduction in the channel from the sealer seat side of the carrier, without additional guiding structures. Upper and lower locking surfaces protruding into the channel can be used to restrict ampoule axial movements. A surface separation of at least ampoule height allows the ampoule to reside between the surfaces. A first advantage with this feature is that ampoule ends are used for axial fixation making superfluous any intermediate structures, such as flanges, recesses, bottle

neck openings, by-pass structures etc., and accordingly makes the carrier compatible with the most pure ampoule designs described. A further advantage is that all forces applied to the ampoule during manufacture, such as in insertion, filling, piston introduction, sealing and removal, are absorbed in the beneficial axial direction, strongly reducing the risks for ampoule damage and plant contamination. Still, releasable locks may make both channel sides accessible for operational steps, both the direct manufacturing steps but also indirect steps, such as probing and ampoule weighing, providing substantial flexibility in use, especially in combination with turnable carrier arrangements, of value in plants for multiple ampoule types or multiple chamber type ampoules. Movable locking surfaces may be complemented with stop surfaces fixed relative each channel to further reduce the risks for inadvertent compression and excessive forces, of value for example when exact tolerances in size or support cannot be guaranteed.--

Please replace the paragraph starting on page 24, line 21 with the following paragraph:

--Figure 4 illustrates schematically main steps in a preferred procedural sequence for manufacture of pre-filled dual-chamber syringe type cartridges. Several steps are conducted with a sterile zone, illustrated with dotted line 40. In a first step 41 syringe barrels are washed and siliconized. The so treated barrels are transmitted through a sterile oven 42 at the exit of which they enter the sterile zone 40. In a piston charging step 43 an intermediate piston is inserted into the barrel to delimit the front and the rear chambers. For example, the piston can be inserted through a front end opening of the barrel to a distance from the front end opening into a sealing engagement with the barrel interior to form a chamber between the piston and front end opening. In charging step 44 the solution to be lyophilized is filled into the front chamber and the solution is lyophilized in step 45. Next 46 the barrel front end is sealed in-situ in the lyophilizing chamber. A solvent for the lyophilized powder is filled into the rear chamber in step 47. In step 48 a rear

piston is inserted into the barrel rear end to confine the solvent in the rear chamber. The preparations in the barrel are now sealed from the surroundings and the prefilled barrel can leave the sterile zone 40. In a final assembly step 49, further components can be added, such as a sealer capping and rear actuating means, preferably by use of a sleeve as intermediate component as described. It is clear that all components charged into the barrel, notably the intermediate piston and the rear piston as well as the solution and the solvent, [has] have to be sluiced into the sterile zone 40 in sterile condition.--

Please replace the paragraph starting on page 25, line 5 with the following paragraph:

--In the above process it is preferred to use the ampoule carrier of the invention in all steps 43 to 48 performed within the sterile zone 40. Due to the carrier versatility it is also possible and preferred to use the carrier in the sterilization oven of step 42 and the carrier can be used in the washing and siliconizing step 41 although these steps can also be conducted with the ampoules in bulk or in blisters. It is generally preferred to remove the ampoules from the carrier before conducting the assembly steps 49. It is generally preferred to turn the ampoules with the carrier upside down between steps 46 and 47, and preferably this is the only turning step until ampoule removal from the carrier. In case the ampoules are of the preferred syringe type described all steps up to 46 inclusive can with preference be conducted [form] from the upper side of the carrier. It is also possible to delay mounting of the sleeve until step 49 outside the sterile zone, which limits the number of components entered into that zone. According to the invention it is possible and preferred to charge the sealers into a carrier rest position, allowing vapor escape, which is preferably done between steps 44 and 45. The in-situ sealing of step 46 is preferably done by axially moving the charged sealers from the rest position into sealing engagement with the barrel front opening.--

In the claims:

Please amend claims 21, 23, 26 and 27 as follows:

--21. (Twice Amended) A process for the manufacture of a prefilled syringe type ampoule having a) a barrel with a front end and a rear end defining an axis therebetween, the barrel having substantially constant cross-section between the front end and the rear end, at least the front end ending in an opening, b) a sealer attached to the front end and sealing the front end opening, c) at least one piston movably and sealingly arranged within the barrel and d) a sleeve extending along at least a part of the barrel, the sleeve having a front part and a rear part, the front part being connected to the sealer, wherein the process comprises the steps of

inserting the piston through the front end opening to a distance from the front end opening into a sealing engagement with the barrel interior to form a chamber between the piston and the front end opening,

filling material into the chamber by passing the material through the front end opening and

sealing the front end opening with the sealer.--

--23. (Twice Amended) The process of claim 21, wherein the sealing step includes the step of inserting a sealer part into the front end opening and contacting the part with [the opening] an interior surface of the barrel adjacent the front end opening.--

--26. (Twice Amended) The process of claim 21, further comprising the step of inserting a second piston through [the] a rear opening at the rear end of the barrel.--

--27. (Twice Amended) The process of claim [21] 26, further comprising the step of performing a filling operation through the rear opening before inserting the second piston.--